

#### **REMARKS/ARGUMENTS**

Reconsideration of the application and entry of the current amendment are respectfully requested. Claims 1-3, 5-10, 13-26 are pending after amendment. Claims 4, 11-12, and 27-38 are cancelled as belonging to non-elected inventions. Claims 7, 9, and 10 are withdrawn as belonging to non-elected species. Claims 14-20 were not included into any Group in the Restriction Requirement, however after amendments to correct claim dependencies, Applicants believe the claims properly fall within the elected Group I. Claims 1-3, 5-10, and 13-26 have been amended. Any amendments in response to claim objections or rejections are discussed in those sections below. Other amendments were done to correct typographical errors, correct claim dependencies, and/or correct antecedent basis. Support for these amendments is found in the specification and claims as originally filed. No new matter has been introduced by these amendments. Applicant reserves the right to pursue any subject matter cancelled or modified by these and any previous amendments.

#### **Election/Restriction**

Applicant acknowledges that the Election of Group I (claims 1-3, 5-10, 13, and 21-26), species C ( $X = 5'$  intron-TSinv-P2inv), and species F ( $Y = 3'$  intron-TSinv-polyA) has been made final. Based on that election, the Examiner has withdrawn claims 7, 9, and 10 for reading on non-elected species. Claims 1-3, 5, 6, 8, 13, and 21-26, species C, and species F are examined in the current Action. Claims 14-20 were not included into any group in the original restriction due to inadvertent errors in claims dependencies for Claims 14 and 18. Claims 14 and 18 have been amended to depend from at least one claim of elected Group I. Applicant requests acknowledgement that these claims properly fall in Group I in the next Office Communication. If the Office disagrees regarding this claim grouping, Applicant requests that the Office clarify the restriction and disposition of these

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claims in the next Action so that the Applicant properly retains all rights to pursue the subject matter of these claims in the current application, and/or any continuing applications.

#### **Information Disclosure Statement**

Applicant acknowledges receipt of initialed copies of the Information Disclosure Statements filed October 15, 2003 (submitted October 9, 2003) and January 2, 2004 (submitted December 30, 2003). Citation of EP 1115870 is incorrectly referred to as EP115878 in the Action. As was noted on the IDS filed October 15, 2003, this is the EPO 'publication' of WO 00/17365 also submitted on the IDS of that date, and therefore may be considered a cumulative citation regarding that subject matter. Also, when downloading EP1115870 from a patent database such as MicroPatent, the WO 00/17365 publication is provided. Odell *et al.* (1991) was inadvertently submitted with both Statements, Applicant apologizes for any confusion.

#### **Claim Objections**

The following claim objections were raised:

- Claims 5, 6, 13, and 21-26 are objected to for depending from non-elected claims; and;
- Claim 23 is objected to for informalities, specifically "of thereof" in the last line.

Claims 5, 6, 13, and 21-26 have been amended to correct claim dependencies. Claim 23 has been amended to delete part (i) which recited "of thereof". Applicant believes these amendments fully address and resolve the claim objections, and respectfully requests that the claim objections be withdrawn in the next Office Communication.

**Rejections under 35 U.S.C. §112, 2<sup>nd</sup> Paragraph:**

Claims 1-3, 5, 6, 8, 13, and 21-26 were rejected under 35 U.S.C. 112 2<sup>nd</sup> paragraph for being indefinite. Specifically:

Claims 1 and 8 are indefinite for reciting “a second gene silencing-recombinase element” in line 6 as no first gene silencing-recombinase element is recited;

Claims 1 and 8 lack proper antecedent basis for “the target gene” recited in the last line;

Claim 13, the term “germline” renders the claim indefinite; and,

Claim 23, the phrase “homologs [of] thereof” renders the claim indefinite.

The rejection will be addressed as it may be applied to Claims 14-20, which have been amended to correct antecedent basis and now should be properly examined with Group I.

Claims 1 and 8 have been amended to delete “gene silencing-”, and now recite “a second recombinase element”. Claims 1 and 8 have further been amended to provide antecedent basis for “the target gene”, specifically part (b)(iii) has been amended to recite “wherein the target sequence is directed to a target gene”. Claim 23 has been amended to delete part (i) reciting “homologs [of] thereof” These amendments obviate the 35 U.S.C. 112 2<sup>nd</sup> paragraph rejection of claims 1-3, 5, 6, 8, and 21-26, therefore it is respectfully requested that the rejection of these claims be withdrawn in the next Office Communication.

Applicant respectfully traverses the conclusion that the term “germline” renders Claim 13 indefinite. The rejection will be addressed as it may be extended to Claims 14-20. Germline is a well-defined term in the art, therefore one of skill in the art knows the metes and bounds of this term (see Appendix A provided herein). Germline is defined as the lineage of cells from which gametes are derived. Because this term is well-defined and understood, it was not redefined in the current application, rather, Applicant provided examples of developmental stages which

provide sources of germline-specific promoters. In the context of the specification, "say" is not an open term, but merely used to indicate the list of examples that followed the term. The term germline is clear and definite, particularly to one of skill in the art, therefore Applicant respectfully requests that the 35 U.S.C. 112 2<sup>nd</sup> paragraph rejection of Claim 13 be withdrawn in the next Office Communication, and not be applied to Claims 14-20.

**Rejections under 35 U.S.C. §103:**

Claims 1-3, 5, 6, 8, 13, 21, 22, and 24-26 were rejected under 35 U.S.C. §103(a) as unpatentable over Smith *et al.* (Nature 407:319-320 2000) in combination with Odell *et al.* (WO 91/09957).

The Action asserts that the Smith *et al.* teach a method for silencing expression of a specific target gene in a cell comprising introduction of a construct that expresses a hairpin RNA comprising an intron, but does not teach a site-specific recombination system.

The Action asserts that Odell *et al.* teach a site-specific recombination system to manipulate exogenous DNA in a plant cell to control expression of the DNA. The site-specific recombination event catalyzed by the Cre recombinase can cause the inversion of a DNA segment that comprises a promoter bound by lox sites in reverse orientation, such that the promoter goes from [sic] an inactive to an active orientation with respect to the coding region to be transcribed.

The Action concludes that it would be obvious to modify the construct of Smith *et al.* to incorporate a site-specific recombination system of Odell *et al.* with the motivation to provide a way to control expression of the exogenous DNA.

Applicant respectfully disagrees. The Office has not shown a *prima facie* case that a person of skill in the art would modify Smith *et al.* by selecting the site-specific recombination of Odell *et al.* Smith *et al.* and Odell *et al.* taken together do not teach the entire invention, that is the creation of a silencing construct by

regulated site-specific recombination. Smith *et al.* not only do not teach a site-specific recombination system, they do not teach any method to control expression of their gene silencing construct, nor do they teach a reason or the desirability to modify their system. In fact, Smith *et al.* teach a method to *enhance the expression* of their construct by incorporating a spliceable intron in a loop between the two hairpin arms, their goal was to increase the frequency of silencing in transgenic events. There is no reason to modify the teachings of Smith *et al.* Just because one of skill in the art *could* modify Smith *et al.* with the teachings of Odell *et al.*, does not prove the case the that one of skill in the art *would* modify Smith *et al.*, and further does not prove would select Odell *et al.* for the modification. The hindsight reconstruction of the invention is an improper standard for an obviousness rejection. Applicant respectfully requests that the 35 U.S.C. §103 rejection of claims 1-3, 5, 6, 8, 13, 21, 22, and 24-26 as unpatentable over Smith *et al.* (2000) in combination with Odell *et al.* (WO 91/09957) be withdrawn in the next Office Communication.

Claim 23 was rejected under 35 U.S.C. §103(a) as unpatentable over Smith *et al.* (Nature 407:319-320 2000) in combination with Odell *et al.* (WO 91/09957), and further in view of Dalmay *et al.* (Cell 101:543-553 2000).

Applicant respectfully disagrees. First, there is no *prima facie* case to combine Smith *et al.* and Odell *et al.* as discussed above, therefore the rejection further combining Dalmay *et al.* is moot. Second, there is no *prima facie* case to add Dalmay *et al.* as none of the references provide a reason to silence a gene required for gene silencing. For example, Smith *et al.* teach a method to enhance gene silencing, not a method to suppress gene silencing. The rejection of Claim 23 under 35 U.S.C. §103(a) constitutes improper hindsight reconstruction of the invention. Applicant respectfully requests that the 35 U.S.C. §103 rejection of claim 23 be withdrawn in the next Office Communication.

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### **CONCLUSION**

In view of the foregoing amendments and remarks, Applicant respectfully submits that the rejections of claims 1-3, 5-10, 13-26 are overcome, and believe that the application is in condition for allowance. Early notice to this effect is solicited. Applicants would appreciate early notification of any and all allowable subject matter. Should further issues arise, the Examiner is encouraged to telephone the undersigned representative to expedite further examination and allowance of the application.

Respectfully submitted,

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